

tumors especially lung cancer which impact outcome. Post-treatment surveillance is therefore practiced on the premise that early detection and timely treatment of recurrences and second primary lung cancers (SPLC) could improve outcome.

Objectives: To determine the outcome of curatively treated HNC patients referred because of the suspicion of SPLC.

Methods: Between 1996 and 2005, patients with HNC referred for respiratory symptoms and/ or radiological abnormalities suspicious for lung cancer were evaluated with radiology and autofluorescence bronchoscopy. Data on patient demographics, smoking, pack years, cancer characteristics and outcome were collected and analyzed.

Results: Fifty-one patients (44 males) with curatively treated N0 HNC were evaluated. Median age was 70 years (range, 63-79), all were current or former smokers of 35 pack years (range, 30-45) and 25 had chronic obstructive lung disease. With a median follow up of 60 months, 8 patients were diagnosed with synchronous and 26 with metachronous SPLC. A total of 42 SPLC were diagnosed; 12 (29%) in the central airways and 30 (71%) parenchymal. Median time to metachronous SPLC was 24 months. Most of SPLC (38/42) were surgically resectable. Five occult cancers detected by AF bronchoscopy were successfully treated with endobronchial therapy. Lung cancer mortality was 24%. Survival of synchronous and metachronous SPLCs was significantly shorter (83 and 144 months) compared to those with HNC alone (240 months) ($p=0.002$).

Conclusion: SPLC has a negative impact on the survival of patients with HNC. Close surveillance with autofluorescence bronchoscopy and CT for SPLC combined with aggressive treatment of early stage lung cancer might be a strategy to improve outcome.

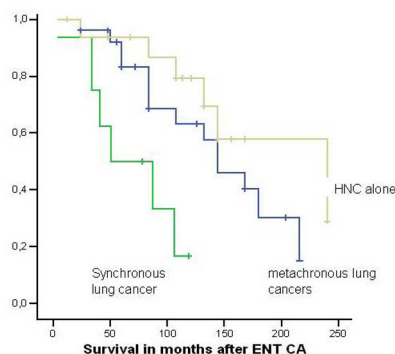


Fig 1: showing survival of HNC patients with synchronous, metachronous lung cancers and without, $p=0.002$

this hospital, usually diagnosed at inoperable or metastatic stages. We pioneered low-cost and free chest CT scan program for this high risk population based on recent data indicating that yearly screening CT scans of chest can lead to early lung cancer diagnosis, and may reduce the lung cancer mortality.

Methods: Low cost screening chest CT scan was advertised through mass media and was offered to general population. We secured outside funding for approximately 300 free screening chest CT scans and these were offered through local primary care providers who were asked to identify individuals at high risk for lung cancer development based on their smoking and/or asbestos exposure history. Overall eligibility criteria for screening CT scan were age 55 and above, with at least 20 pack-year smoking history. All CT scans were done at Harbor Hospital Radiology Department, and results were classified as negative, indeterminate or suspicious. Indeterminate or suspicious results were reviewed and discussed at the multidisciplinary Lung Tumor conference and follow-up recommendation was issued according to the Early Lung Cancer Action Program (ELCAP) guidelines.

Results: A total of 492 patients underwent screening chest CT scans between 3/2003 and 2/2006. Median age of patients was 57 years (33-80), with 261(53%) women and 231(47%) men. The majority of screened population was Caucasian (68%), with 20% African Americans and small number of Asians (3%). More than 95% of the patients were current or ex-smokers, with median of 33-pack year smoking history (3-200). Among 459 smokers, 133 (29%) were former smokers with median of 10-year smoking cessation history (1mo to 40 years). Initial CT scan results were reported as normal in 258 (52%) and indeterminate in 234(48%). Non-small cell lung cancer was diagnosed in 8 patients (1.6%), who were referred to appropriate disciplines for staging and treatment. Three out of 8 patients were found to have stage I/II NSCLC and underwent surgical resection. Total of 10 out of 492 patients were diagnosed with cancer, two additional patients were incidentally found with other types of cancers, one laryngeal and another with pancreatic cancer.

Conclusion: Eight cases of NSCLC were diagnosed after screening 492 high-risk populations at a community hospital in downtown Baltimore. Among them, three patients (38%) were found to have early stage lung cancer and were offered curative resection. Following our experience, many other local community hospitals engaged in similar programs to provide low cost chest CT scans for early lung cancer detection. In our limited experience, screening chest CT scans yielded relatively more early stage lung cancers than our historical control. The usefulness of this approach remains to be established with ongoing large multicenter randomized trials sponsored by National Cancer Institute and ELCAP.

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Prevention and Early Detection Posters, Mon, Sept 3

Lung cancer screening experience at a community hospital in Baltimore, Maryland

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Background: Harbor Hospital is located in downtown Baltimore, serving largely blue-collar workers with very high smoking prevalence. Non-small cell lung cancer is the most common malignancy seen at

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Bronchial epithelial proliferation measured by Ki-67 is related to current smoking and sex but not to lung cancer or chronic obstructive pulmonary disease

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Background: Bronchial epithelial proliferation as measured by Ki-67 immunostaining is a biologically plausible intermediate endpoint biomarker of lung cancer risk, but has not been validated. We designed a study to determine factors associated with increased bronchial epithelial proliferation and whether increased epithelial proliferation is associated with endobronchial dysplasia, chronic obstructive pulmonary disease or lung cancer.

Methods: Cross-sectional study of 113 subjects undergoing white light and autofluorescence bronchoscopy; 27 never smokers, 27 current or ex-smokers with normal spirometry, 31 current or ex-smokers with COPD and 28 current, ex- or never smokers with lung cancer. Ki-67 expression was determined by immunohistochemistry on all evaluable biopsy sites without carcinoma. A Ki-67 index was defined as the percent of cells expressing Ki-67. Relationships between Ki-67 index and demographic variables, smoking, histology and the presence of COPD and/or lung cancer were determined.

Results: Results for both maximal and mean Ki-67 index are similar, so only the former are reported. Average maximal Ki-67 index was higher in current smokers than either ex-smokers or never smokers (48.0% vs 30.6% vs 22.6%; $p < 0.001$). Males had higher Ki-67 index than females, (39.9% vs 23.6% $p < 0.001$). Compared to subjects without disease (Ki67 index = 30.0%) maximal Ki-67 index was not significantly elevated ($p = 0.44$) in subjects with either lung cancer (Ki67 = 39.1%) or COPD (Ki67 = 38.9%)

Conclusions: Current smoking and gender are major determinants of Ki-67 index. No increase in Ki-67 index was found in the non-malignant epithelium of patients with lung cancer or COPD. Although Ki-67 index may provide insight into the short-term effects of chemoprevention agents on cell proliferation, its lack of association with lung cancer or COPD raise question about its utility as a surrogate endpoint in clinical trials.

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Epidermal Growth Factor Receptor (EGFR) inhibition with gefitinib is synergistic with prostacyclin synthase overexpression in chemopreventing murine lung cancer

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Background: Chemically induced murine adenocarcinomas contain many of the same histological and genetic alterations found in human adenocarcinomas, affirming the importance of murine tumorigenesis models. Increased pulmonary PGI₂ (prostacyclin) by lung-specific overexpression of prostacyclin synthase (PGIS) chemoprevents lung cancer in chemically induced and cigarette smoke exposure models, suggesting that PGI₂ plays a role in the development of NSCLC. Alterations in EGFR by mutation or increased copy number are identified in a subset of lung cancers, and targeted therapies with tyrosine kinase inhibitors (TKIs) are currently in clinical use for NSCLC. We hypothesized that the TKI gefitinib would provide synergistic chemoprevention of murine lung cancer when combined with PGIS overexpression.

Methods: PGIS overexpressors and their wild-type littermates were given a single intraperitoneal (i.p.) injection of urethane. After one week, body-weight based i.p. injections of gefitinib were given in doses of 50mg/kg (n=45), 100mg/kg (n=41) or vehicle alone (tween 80R, n=43) three times per week. Serial body weights were followed during

the experiment, and at the time of sacrifice (18 weeks after urethane) lung tissue and tumors were collected. Lung tissue was snap frozen, stored in formalin or RNA later, or immediately used for analysis of PGE₂ and 6-keto PGF₁α (the stable metabolite of PGI₂) eicosanoid levels. Additional overexpressing and wild-type animals (n=12 in each group) received gefitinib for two weeks only, after which lung tissue was harvested for studies to determine if EGFR inhibition was successful. Western blots for p-Erk, p-Src, and p-Akt were performed on lung homogenates from all treatment groups.

Results: PGIS overexpressors, when compared with transgene negative littermates, showed significant decreases in tumor multiplicity consistent with our prior studies. A further reduction in tumor multiplicity (1.13 ± 0.29 vs. 2.29 ± 0.32 tumors/mouse, $p = 0.0149$) was observed in the 50mg/kg treatment group versus the vehicle alone. No additional effects were realized in the 100mg/kg treatment group (2.00 ± 0.32 tumors/mouse, $p = 0.5340$). No significant differences in tumor burden or eicosanoid levels were observed among the experimental groups. Analysis of p-Erk, p-Src, and p-Akt in PGIS treated animals showed decreases in the 50mg/kg treatment group, while the 100mg/kg group showed a paradoxical return of p-Src. Western blot analyses of p-Ten and cleaved caspase 3 continue to be performed.

Conclusions: Animals tolerated i.p. injection at doses of 50mg/kg and 100mg/kg. Lung homogenates from gefitinib-treated mice showed a decrease in p-EGFR following EGF exposure, demonstrating successful inhibition of EGFR in our model. At a dose of 50mg/kg, treatment with gefitinib was synergistic with PGIS overexpression in decreasing tumor multiplicity. The observed increases in p-Src in both wild-type and PGIS mice in the 100mg/kg treatment group suggest a mechanism of adaptation to EGFR inhibition. Future investigations into the synergy of prostacyclin manipulation and EGFR inhibition are planned.

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Individual screening of lung cancer in france: results of EDIFICE study

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Objectives: EDIFICE study was aimed at improving knowledge of the French population adherence to screening tests for the four most frequent cancers: breast, colon-rectum, prostate and lung cancers. The results pertaining to lung cancer are summarised below.

Methods: This was an observational survey conducted in France among a representative sample of 1 504 subjects aged 40 to 75 years without history of cancer and among a representative sample of 600 general practitioners (GPs).

Results: Individual screening for lung cancer using chest radiography had been performed by 6% of subjects (of whom 51% were women). Compared with the unscreened subjects, more screened subjects were smokers (33% versus 23%; $p < 0.05$). Cancer screening had often been initiated by the GP (22%) or the company doctor (21%). Regarding the screened subjects' profile, mean age was 54.5 years; their socio-profes-